Evidence Based Medicine:
Alendronate vs Raloxifene in Postmenopausal Osteoporosis

by Tacara Soones

Case:	*83F former smoker with h/o anemia and PUD who was admitted to senior medicine for multiple falls 2/2 iron deficiency anemia.*
Studies:	*-DEXA (2004): lumbar spine (-2.5), total hip (-1.7) and distal radius (-1.2).* *-Xray of thoracic spine- Old compression fracture at T8 and new compression fractures at T4 and T6.* *-Xray lumbar spine showed degenerative changes of the apophyseal joints.*
Treatment:	*She was started on Fosamax (alendronate) for postmenopausal osteoporosis.* *Is there evidence to support a bisphosphonate over a SERM in preventing fractures?*

Alendronate produces greater effects than raloxifene on bone density and bone turnover in postmenopausal women with low bone density: results of the EFFECT (*EF*ficacy of *F*osamax versus EVISTA *C*omparison *T*rial) International. Sambrook, Gueusens et al. *J Intern Med* 2004; 255: 503-511.

Study Design	• randomized, double-masked, double-dummy multicenter international trial
Population	• women with postmenopausal osteoporosis seen at 50 centers in 16 countries
Inclusion	• t-score ≤ 2
Exclusion	• b/l hip replacement • history of DVT • marked hypertriglyceridemia in response to estrogen • esophageal stricture or achalasia • bone-active therapy within 1 year • medical conditions that could affect bone metabolism
Intervention	• alendronate 70mg weekly plus daily placebo identical to raloxifene • raloxifene 60mg daily plus weekly placebo identical to alendronate
Outcomes	• bone mineral density at 3, 6 and 12 months • markers of bone turnover- bone specific alk phos, N-telopeptide (Cr corrected)

Are the results of the study valid?

Criteria	Yes	No
Randomized	√	
Subjects accounted for	√	
Follow-up complete	√	
Intention to treat	√	√

Criteria	Yes	No
Double-blind	√	
Demographic homogeneity	√	
Treatment homogeneity	√	

Results

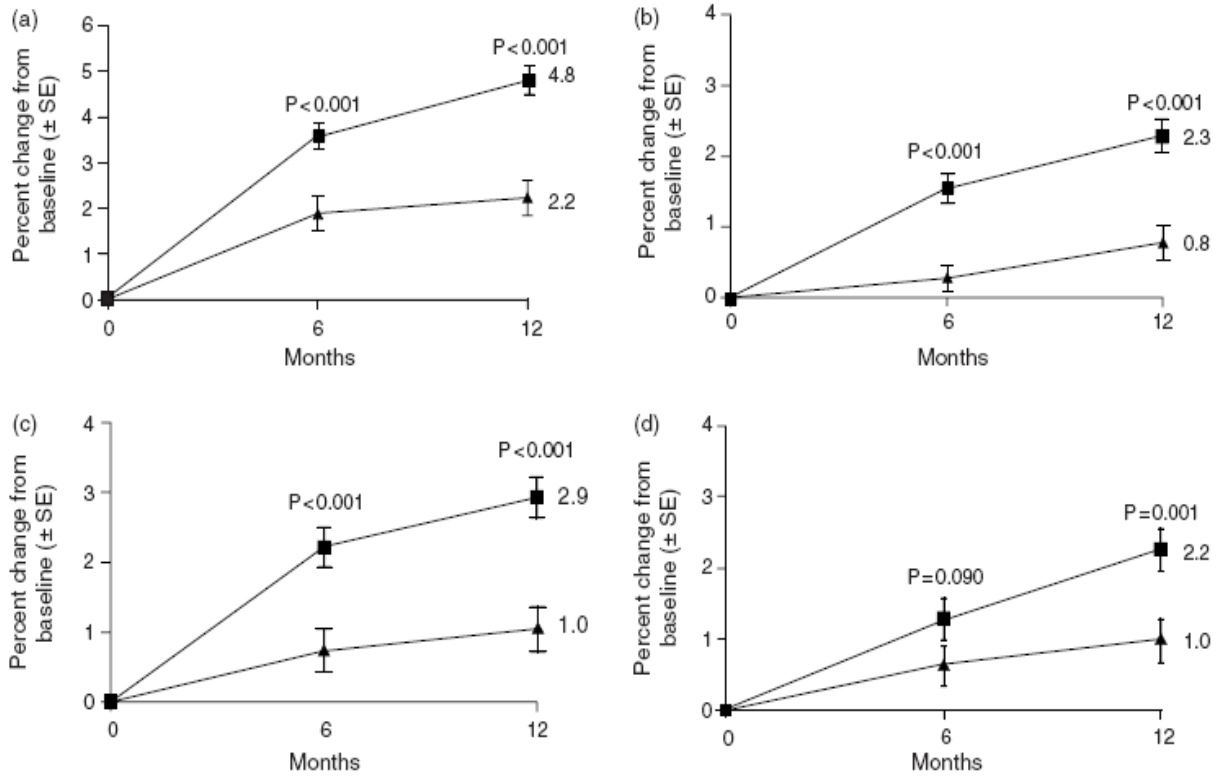

Fig. 2 (a) Changes in bone mineral density (BMD) at lumbar spine. (b) Changes in BMD at total hip. (c) Changes in BMD at hip trochanter. (d) Changes in BMD at femoral neck. The alendronate group experienced greater increases in BMD compared with the raloxifene group at 6 and 12 months at both the hip and spine. ■ alendronate, ▲ raloxifene, *P*-value for between treatment group comparison.

- More subjects taking alendronate maintained or increased their BMD (87% vs 73%, $p<0.001$).
- Markers of bone turnover decreased more in the alendronate group (68% vs 28%, $p<0.001$).
- "Clinically apparent" fractures: 6 fractures in 6 patients on aledronate, 8 fractures in 5 patients on raloxifene. 1 hip fracture in the raloxifene group.

Will the results affect treatment?

- Patient is described by patient population, inclusion and exclusion criteria.
- Increased BMD ≠ decreased hip fracture risk, though the two are correlated. What is a meaningful percent change in BMD?
- Potential benefit of decreased morbidity and mortality 2/2 hip fractures outweighs the potential costs associated with alendronate over raloxifene. Alendronate is cheaper. The side effect profiles are similar.
- Decision: Offer this patient alendronate with the understanding that this study shows an increase in bone density, not a decrease in fracture risk, and that it might not be clinically significant.

Search Methods

- Medline search using the PICO format.

PICO strategy	#	**Searches**	**Results**
Patient population: post menopausal women with osteoporosis	1	Osteoporosis, postmenopausal/	8199
Intervention: fosamax	2	Alendronate/	1822
Comparison: evista	3	Raloxifene/	1700
Outcome	4	Bone Density/	27779
Outcome	5	Fracture.mp.	94812
	6	1 and 2 and 3 and 4 and 5	19
Outcome: either changes in bone density or fracture incidence	7	4 or 5	117271
	8	1 and 2 and 3 and 7	55
Type of study: RCT	9	Randomized Controlled Trial/	263468
Final results	10	8 and 9	7

Limitations

- If there are other meaningful predictors of fracture risk on which alendronate and raloxifene are compared, these were missed by my outcomes criteria.